IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF CALIFORNIA
SAN JOSE DIVISION

GENENTECH, INC.,

Plaintiff and Counterclaim Defendant

v.

THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA,

Defendant and Counterclaimant

Case No. 5:10-cv-02037-LHK (PSG)

DECLARATION OF EDWARD LENTZ

WITH PROPOSED REDACTIONS

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I. INTRODUCTION AND BACKGROUND

1. I have personal knowledge of certain facts stated herein and, if called to do so, could and would testify competently thereto under oath.

2. I have been retained as an independent expert witness on behalf of the University of Pennsylvania. I have been asked to prepare reports on, among other things, questions relating to damages, inducing infringement, and willfulness.

3. I have been asked to consider questions relating to customs and practice in the pharmaceutical and biotechnology industry.

4. When I refer to the "Industry" in this declaration, I am referring to the pharmaceutical and biotechnology industry. When I refer to a "custom" or "practice" in the Industry in this report, I am referring to customs, usages, or practices in the Industry applicable to my discussion of an agreement or practice.

5. I received my B.A. in Biology from Fordham University in 1976, my M.A. in Life Sciences from Indiana State University in 1977, and my J.D. from Villanova University in 1980. I spent close to 20 years of my legal career as an attorney at SmithKline Beecham (now GlaxoSmithKline), one of the largest pharmaceutical companies in the world. I was ultimately appointed Senior Vice President and General Counsel (United States). My responsibilities included negotiations and litigations involving bio/pharmaceutical patents, license agreements, and other technology transfer agreements; drafting, interpreting, and opining on license agreements; assessing patentability and freedom to operate and preparing opinions relating to those subjects; reviewing agreements and freedom to operate opinions prepared by other attorneys; and overseeing intellectual property litigation directly managed by other attorneys.

6. In 2001, I left GlaxoSmithKline to join the intellectual property group at Morgan Lewis & Bockius. There, I performed a full range of patent legal services including in such areas as are summarized above. Two years later, in 2003, I started my own private legal practice. The scope and activities of this practice are and have been substantially the same as they were while at Morgan Lewis & Bockius although my client list is now more heavily weighted towards early stage pharmaceutical and biotechnology companies than large ones. Thus, my practice continues

to include negotiation and drafting of patent and technology-related agreements and the preparation of freedom to operate opinions. My experience includes matters in the field of biopharmaceuticals and oncology. On certain technology transfer agreement matters, I have been adverse to universities and on others I have represented universities.

7. I have served as an arbitrator with the American Arbitration Association, as well as adjunct faculty at Albany Law School, where I have taught classes on patent and technology licensing and on United States and European patent law.

8. I have served on the Board of Directors of the American Intellectual Property Law Association, and was the chair of its Biotechnology Committee. I also served as Vice President, a Director, and a member of the Executive Committee of the Intellectual Property Owners Association. I have also served on the Executive Committee of the Legal Committee of PhRMA, the primary trade organization for research-based pharmaceutical companies. I have also presented at conferences on issues relating to intellectual property and the Industry, including conferences sponsored by the American Intellectual Property Law Association, the American Association for the Advancement of Science, and the American Conference Institute.

9. A list of publications I have authored in the last ten years is included in my attached *curriculum vitae*. Ex. 2 [Curriculum Vitae]. A list of litigation matters in which I testified at trial or deposition is also included. *Id.* I am being compensated based upon actual hours expended on this matter at my normal hourly rate for expert engagements, which is $475/hr. Payment is not contingent upon my findings or opinions or upon the outcome of this matter.

II. MATERIALS CONSIDERED

10. My opinions are based upon (a) my education training and experience, (b) documentary evidence, and (c) deposition testimony.

11. A list of documents I have considered in preparing this report is attached as Ex. 3. Examples of the types of information available to me include the following:

- legal documents (e.g., Complaint; Answer; Disclosure of Asserted Claims and Infringement Contentions; Responses to Interrogatories; etc.);
- patents (e.g., the '752 Patent);

- deposition transcripts;
- documents produced by the University (e.g., various license and settlement agreements);
- documents produced by Genentech (e.g., various Genentech presentations; sales data; financial statements; licenses; etc.);
- information independently obtained (e.g., information from Genentech's website; general product information; etc.); and
- access to document databases (i.e., remote access to all the University-produced documents and Genentech-produced documents in this matter).

12. In addition, I have had discussions with Dr. Evan Dick (Former VP in charge of business development at Fulcrum Pharmaceuticals LLC ("Fulcrum")) regarding Fulcrum/Ception's business-related licensing practices. I have also had discussions with University's other experts in this matter, including Dr. Stuart Aaronson, Dr. Vandana Sharma, and Dr. Ryan Sullivan.

III. GENENTECH'S ACCUSED PRODUCT

13. Herceptin® (trastuzumab) was developed as a therapeutic antibody targeted to the human p185 (HER2+) cell surface protein.[1] Herceptin is a [redacted]

14. On September 25, 1998, Herceptin was approved for use in metastatic breast cancer treatment for patients who have tumors that overexpress at certain levels the HER2 protein. Ex. 5 [FDA, Herceptin Approval Letter, 9/25/1998]. In December 2000, enrollment began of two Phase III clinical trials evaluating the potential use of Herceptin for the adjuvant treatment of early-stage HER2-positive breast cancer (the NSABP and NCCTG trials). Ex. 6 [Herceptin Development Timeline].

15. In May 2005, data from a joint analysis of these trials was released evaluating the addition of Herceptin to standard adjuvant therapy for patients with early-stage HER2-positive breast cancer. Ex. 6 [Herceptin Development Timeline]. These trials were considered a resounding success demonstrating high efficacy and a tremendous potential market for Herceptin.

[1] http://www.gene.com/gene/research/focusareas/oncology/herpathwayexpertise.html.

See Ex. 7 [Perez Press Release (lead investigator on the adjuvant trials stated "[t]he reduction in disease recurrence observed in these trials was the largest improvement I've seen in breast cancer clinical research.")]; Ex. 8 [Hortobaygi, NEJM 2005 at 1735 ("results are simply stunning")]; Ex. 9 [GNE00272724-272725]; Ex. 10, [GNE00429755-429792 at -778]; Ex. 11 [GNE00429875-429893 at -884-85]; Ex. 12 [GNE00431465]; Ex. 13 [GNE00123602-123607 at -606];

[redacted]

16. On November 16, 2006, Herceptin was approved for use in adjuvant breast cancer treatment in combination with doxorubicin, cyclophosphamide, and paclitaxel for patients with HER2-overexpressing, node-positive breast cancer.[2] Ex. 18 [FDA, Herceptin Approval Letter,

[2] The original approval for the adjuvant breast cancer indication was limited to node positive patients and was later expanded to include node negative patients. Ex. 19 [FDA, Herceptin Approval Letter, 5/22/2008]. As of November 2006, clinical study data from the other pivotal trials that were ultimately used to support the current scope of the adjuvant breast cancer trials were also available. These trials are commonly referred to as HERA and BCIRG 0006 trials: "In May 2005, an interim analysis from an adjuvant trial called HERA (HERceptin Adjuvant) conducted internationally by Roche and the Breast International Group (BIG) was reported at the ASCO meeting, and these results were published in the *New England Journal of Medicine* in

11/26/2006]. Herceptin received additional approvals for adjuvant treatment as a single agent on January 18, 2008 and with other drug combinations on May 22, 2008. Exs. 19, 21 [FDA, Herceptin Approval Letters, 1/18/2008 and 5/22/2008].

17. The Herceptin website, lists the four studies that led to adjuvant approval as evidencing a "52% higher chance of remaining cancer free longer," a "46% higher chance of remaining cancer free longer," and a "33% chance of remaining cancer free longer."[3]

IV. REASONABLE ROYALTY OPINIONS

A. Framework of Analysis

18. I understand that in patent infringement litigation, the patent laws provide for damages to a prevailing patent holder in an amount that compensates for the infringement: "[u]pon finding for the claimant the court shall award the claimant damages adequate to compensate for the infringement, but in no event less than a reasonable royalty for the use made of the invention by the infringer, together with interest and costs as fixed by the court."[4] A reasonable royalty is determined through an analysis of what a willing licensor and a willing licensee would have bargained for during an arm's-length, hypothetical negotiation occurring at the time of first infringement.[5] A number of factors may be considered in evaluating such negotiations, including the customs and practices in the Industry.[6]

October 2005. An international study supported by Sanofi-Aventis and Genentech, and conducted by the Breast Cancer International Research Group (BCIRG), also showed that treatment with Herceptin in addition to or following chemotherapy improved disease-free survival. These data were announced in September 2005 and presented at the San Antonio Breast Cancer Symposium (SABCS) in December 2005." Ex. 20 [February 15, 2006 Genentech Press Release].

It is typical in the Industry to seek expansion of approved indications for use at a later date. The parties to a hypothetical negotiation at the time of first infringement would have taken into account all of the clinical data and its impact on the scope of the eventual indication.

[3] http://www.herceptin.com/breast/adjuvant/.

[4] 35 U.S.C. § 284. I note that because the '752 patent only has method claims, no notice is necessary for past damages to accrue.

[5] *See, e.g., Rite-Hite Corp. v. Kelley Co., Inc.*, 56 F.3d 1538, 1554 (Fed. Cir. 1995).

[6] *See, e.g., Georgia-Pacific Corporation v. United States Plywood Corp.*, 318 F. Supp. 1116 (S.D.N.Y. 1970).

19. I have been asked to provide my opinion with respect to customs and practices in the Industry for licensing, including how such customs and practices impact: (1) the type and scope of the license; (2) the time of the hypothetical negotiation; and (3) the royalty base.

B. Licenses to Method Patents

20. It is common for pharmaceutical companies to take licenses to method patents owned by academic institutions such as universities. The research of academic institutions often generates technology that can benefit society and be profitable in commercial ventures. However, pharmaceutical companies are better equipped than academic institutions to commercialize pharmaceutical products. Accordingly, license agreements allow technologies to be commercialized by entities with the experience and infrastructure to bring products to market. Genentech's corporate designee on licensing, Mr. Schwartz, testified that [redacted]

21. New methods of treatment potentially provide significant value enhancement because they can open up new patient populations. Licensees may desire licenses to patents covering such methods because they provide freedom to operate and additional patent protection. Licensors such as academic institutions or commercial entities that do not intend to commercialize a patented method may offer a license to a method patent because it will result in greater use of the technology as well as additional revenue to fund further research. Thus, it is common for a license to a method patent to appeal to both pharmaceutical companies and academic institutions.

22. The parties have produced examples of licenses to method patents in this litigation. [redacted]

23. Compensation for patent licenses in the Industry often comprises an upfront fee, milestone fees, and a running royalty, often called an earned royalty. The parties have produced

numerous licenses in this case with these types of compensation. An earned royalty is typically a defined percentage of actual net sales of licensed products or services. Compensation for patent licenses in the Industry also can include license maintenance fees, minimum royalties, or both. In the case of patent licenses granted by universities to commercial entities, such license agreements typically require the licensee to reimburse the university for past and future patent-related expenses. *See, e.g.,* [redacted]

24. In the case of patent licenses for products that are already commercialized, it is reasonable for license compensation to be weighted very heavily towards a running royalty for a number of reasons. First, upfront fees and milestone payments are generally intended to allow the licensor to realize value before commercialization begins, and even if the product fails in development, and to allow the licensee to spread compensation and, therefore, risk, over the period of time during which the product is undergoing development. In the case of a commercialized product, these considerations don't apply. Second, because the net sales and profitability of a commercialized product are easier to estimate, the absolute value of a running royalty can be more readily estimated. Third, under a running royalty structure, the licensee only pays a royalty if and when the licensed product sells. This is a fair allocation of risk between licensor and licensee because compensation is reflective of the actual success of the licensed technology.

25. By the time of the hypothetical negotiation in the present case, the risk of development failure was not present. In light of the foregoing, custom in the Industry would be for the compensation in a hypothetical negotiation for the '752 Patent to consist of a running royalty.

26. A running royalty is also consistent with licensing research finding that 83% of all biopharmaceutical licenses included running royalty rates that were either flat or tiered, and that 91% of royalty rates are paid as a percentage of either gross or net sales. Ex. 26 [Licensing Executives Society, Global BioPharmaceutical Royalty Rates & Deal Terms Survey, 9/2010 at 29-30, 34]. This research also showed that less than 6% of biopharmaceutical license deals were for flat fee compensation. *Id.* at 151 ("Flat fee" is included under "Other" which garnered 6% of

responses, and included flat fee, profit sharing, gross sublicense revenue, one time payment, gross margin percentage, and usage rates)].

27. Strong evidence that Genentech would have sought a running royalty comes from the fact that in [redacted] But as discussed below, [redacted]

C. Time of Hypothetical Negotiation

28. I understand that Genentech has taken the position that activities relating to obtaining approval of Herceptin for the adjuvant breast cancer indication would not have infringed the '752 Patent because such activities would have been exempt from infringement under 35 U.S.C. 271(e)(1). Ex. 27 [Genentech Response to Interrogatory No. 1 at 5]; *see also* Ex. 28 [Dkt. No. 303]. Herceptin was approved for the use in the adjuvant context in November 2006. Ex. 18 [FDA, Herceptin Approval Letter, 11/26/2006]. Genentech began selling Herceptin for adjuvant use under this approval in the fourth quarter of 2006. Ex. 29 [GNE00417987-GNE00417992 at -991]. It is my opinion that the conservative time to be applied to the hypothetical negotiation is just prior to FDA approval for adjuvant treatment with Herceptin, which occurred on November 26, 2006.

D. Royalty Base

29. A royalty base is the portion of the net sales of products and services upon which a running royalty is based. In a license to a method of use patent applicable to an existing pharmaceutical product, in the Industry the royalty base is typically sales of the pharmaceutical product to the addressable population. In this case, the addressable population is patients who receive Herceptin in adjuvant therapy after resection (the "Adjuvant Population").

30. The use of this royalty base coupled with a percentage royalty is accepted by the Industry as the standard way to reflect the commercial contribution of the patented technology to

the value of the product—especially where the demand for the product is based at least in part upon the patented technology. There are a number of reasons why this Industry standard would be applied to the hypothetical negotiation involving the '752 Patent.

31. Pharmaceutical companies in the ordinary course of business keep records on the sales of drugs. If a royalty base were apportioned, such as by relying only upon sales of product shown to be effective in treated patients (or benefiting from a specific mechanism), then tests would need to be conducted to determine whether a licensed technology was effective in a given treated patient or whether the given patient benefitted from a specific mechanism. This would create significant and unnecessary additional expense and complexity. First, such tests would have to actually exist. Then, doctors and patients would have to be willing to administer such additional tests. Even if these burdens were overcome, royalty payments would be unreasonably delayed as it might be years between the first sale of a drug and the ultimate determination of whether the licensed technology was effective in any particular patient. For these reasons, a license based upon pharmaceutical efficacy would be impractical in the Industry.

32. I have never seen a situation in which payments for drugs are contingent on efficacy. In the Industry, it is understood that a given drug will likely not be effective in a certain subset of patients for whom the drug is indicated, either because they will get sick no matter what, or would not have gotten sick regardless of the drug. However, the same price is charged to all patients and, in the case of patent licenses, the same royalty is paid regardless of whether or not the drug was effective in a given set of patients.

33. A negotiation position in which payment would only occur for actual efficacy would not accurately reflect the value of the patented technology. Drugs for life threatening conditions are purchased because they provide an opportunity for benefit. For example, there is a population of women who will receive adjuvant Herceptin therapy who may still develop a recurrence of their cancer. There is also a population of women who will never have their breast cancer recur even if they do not use Herceptin, but both are induced to use Herceptin because of the opportunity to avoid recurrence. In other words, the efficacy that is shown in one group of

women is what causes other groups of women to use the drug, regardless of whether it will actually be effective for them.

34. In addition to paying royalties on the entire addressable population, persons working in the Industry also recognize that in certain circumstances royalties are payable even when an applicable patent right does not exist. For example, in certain licenses, [redacted]

1. Sales For Use In Adjuvant Population

35. In the present case, as discussed above, the Court construed "an individual in need," as used in the claims of the '752 Patent, to include "an individual who…has had her/his neu-associated breast cancer tumors removed by surgical resection, or has been diagnosed as having neu-associated breast cancer enter remission." Ex. 38 [Order Construing Disputed Claim Terms of U.S. Patent No. 6,733,752, 5/9/2011 at 15-16]. I understand that the population of patients accused of infringement in this case are woman diagnosed with primary breast cancer (*i.e.*, they are not diagnosed with metastatic breast cancer, not M1) who have been treated by removal of their breast tumor(s) (the "Adjuvant Population").[7] *See* Ex. 39 [Third amended infringement contentions].

[7] I understand that Genentech has produced survey information in this case by which the sales to the Adjuvant Population has been calculated. Obtaining survey information for the purposes of answering business questions is an accepted standard practice for the Industry.

A royalty base founded upon product sales to the Adjuvant Population is consistent with the royalty bases typically used in the Industry, as Genentech itself acknowledges: "[w]e have obtained licenses from various parties that we deem to be necessary or desirable for the manufacture, use, or sale of our products. These licenses (both exclusive and non-exclusive) generally require us to pay royalties to the parties on product sales." Ex. 40 [Genentech, Form 10-K, 2008 at 9]. Simply put, in the Industry patients pay for the opportunity to potentially benefit from treatment, not for guaranteed results.

37. For example, Genentech relies on studies that led to adjuvant approval as evidencing a "52% higher chance of remaining cancer free longer," a" 46% higher chance of remaining cancer free longer," and a "33% chance of remaining cancer free longer."[8]

38. I am not aware of support for the notion of a royalty base based on patients for whom treatment has actual efficacy. In other words, potential benefit is a driver of Herceptin sales, regardless of whether it is effective for any individual patient. Any royalty base in a hypothetical negotiation would similarly have been for the opportunity of potentially benefiting from the claimed therapeutic strategy—*i.e.* it would include the Adjuvant Population.

[8] http://www.herceptin.com/breast/adjuvant/.

39. The '752 Patent proposes that its strategy of inhibiting development of breast cells into breast cancer cells (claim 1) can prevent "recurrence" of cancer. Ex. 1 ['752 Patent, col. 8:45-47 ("Prevention of metastasis or recurrence is feasibly by administering anti-p185 antibodies.")]. Genentech uses the concepts of preventing the risk of "recurrence" and remaining "cancer free" as the basis for marketing Herceptin in the adjuvant indication to the Adjuvant Population as a whole: "Increase the Chance of Staying Cancer-Free Longer with Herceptin as Adjuvant Treatment;" "1 year of Herceptin lowered the risk of HER2+ breast cancer returning;" "Women who received 1 year of Herceptin had a lower risk of cancer returning than women who did not receive Herceptin;" and "Women who received Herceptin with chemotherapy had a 52% lower risk of breast cancer returning compared with those who received chemotherapy alone." *See, e.g.*, Ex. 41 [GNE00020189-239 at -189, -210]; *see also* generally Sharma Decl., Genentech Marketing Appendix.

40. Genentech witnesses have confirmed [redacted]

41. I understand that the breast cells that the University claims are inhibited from developing into breast cancer cells when Herceptin is administered to the Adjuvant Population are isolated tumor cells ("ITCs"), also known as disseminated tumor cells, present at distant locations in the body that have not fully developed into cancer cells. I understand that Herceptin achieves its results in adjuvant therapy by acting on ITCs. A number of Genentech witnesses have provided relevant testimony on this subject:

- Dr. Robert Cohen, a Senior Fellow at Genentech, gave the following testimony:

[redacted]

[redacted]Dr. Howard Stern, a scientist at Genentech involved in Herceptin, gave the following testimony[redacted]

[redacted]

[redacted]

- Genentech's 30(b)(6)[9] regarding "whether Trastuzumab acts or may act on isolated tumor cells" gave the following testimony:
  - Dr. Elli Guardino, a medical director at Genentech, testified that "[redacted] at 456:18-457:9.
  - Dr. Stuart Lutzker, the vice president of early clinical development at Genentech, and an oncologist, testified that "[redacted] According to the witness, Dr. Lutzker "[redacted] Dr. Lutzker pointed to publications by Romond and Piccart in the New England Journal of Medicine discussing the pivotal trials that led to adjuvant approval [redacted] *Id.* at 459:1-13.

42. Dr. Cohen also gave [redacted]

43. I understand that ITCs are detected in a portion of the Adjuvant Population. *See, e.g.,* Ex. 46 [Braun, et al. "A Pooled Analysis of Bone Marrow Micrometastasis in Breast Cancer,"

[9] Ex. 44 [Cohen II Depo.] at 437:1-25.

New England Journal of Medicine, 2005 at 353:793-802]; Ex. 47 [Janni, et al. "Persistence of Disseminated Tumor Cells in the Bone Marrow of Breast Cancer Patients Predicts Increased Risk for Relapse--A European Pooled Analysis," Clinical Cancer Research, 17:2967-2976, 2011 at 2968]; Ex. 48 [Solomayer, et al. "Comparison of HER2 status between primary tumor and disseminated tumor cells in primary breast cancer patients" Breast Cancer Research and Treatment, 2006 at 98:179-184]. In my opinion, it would not be proper to limit the royalty base to just sales to the portion of the Adjuvant Population in which ITCs might be detected in a survey. I understand that Drs. Sharma, Aaronson and Jensen conclude that it is accepted as more likely than not at the beginning of Herceptin treatment that the ITCs at issue in this case are present throughout the Adjuvant Population because of the limits of detection technology.

[redacted] Genentech makes no effort to promote such testing to identify a more focused patient population more likely to benefit from Herceptin in the adjuvant context. Similarly, Genentech has made no effort to limit the adjuvant indication to patients without detectable ITCs: [redacted]

45. Limiting the royalty base to patients in whom ITCs are detected is a licensing structure I have never encountered in the Industry. It would be analogous to not paying a royalty on a sale of an antibiotic to a patient that has not been tested to confirm the presence of the bacterial pathogen for which the antibiotic is indicated and for which the use of the antibiotic is patented.

2. ADCC v. Anti-Signaling Effects

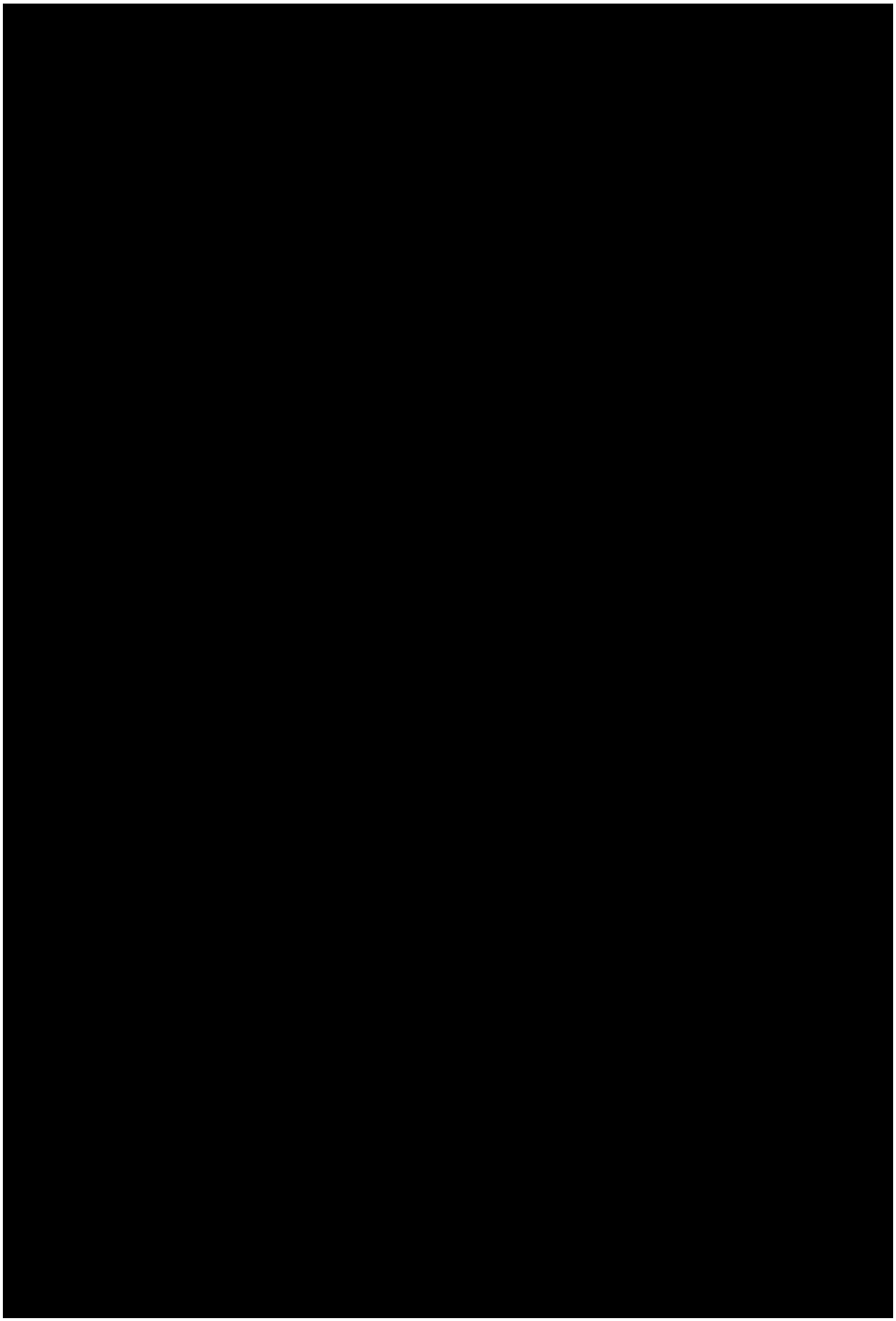
46. Genentech [redacted]

[redacted]

ADCC infringes the '752 Patent. Ex. 39 [Third amended infringement contentions]. In my opinion, it would not be proper to limit the royalty base to exclude those patients in which ADCC might be contributing to effect.

48. Genentec[redacted]

Genentech scientists confirm [redacted]



50. Dr. Dennis Slamon, one of the leaders of one of the trials that supported the adjuvant indication testified that the anti-signaling effect of Herceptin is the "dominant" effect in the adjuvant context:

> Q The BCIRG 006 study, that was a study of adjuvant therapy; is that correct?
>
> A Yes.
>
> Q And it involved the administration of Herceptin with different modalities of chemotherapeutics; is that correct?
>
> A Yes.
>
> Q In those studies, do you have a view as to the -- strike that.
>
> In adjuvant studies, is it your belief that the efficacy shown in those studies is driven by Herceptin's antisignaling effects?
>
> A Yes. That does not mean there aren't other effects, but that's what I think is the dominant effect.

Ex. 57 [Slamon Depo.] at 47:8-22.[10]

[redacted] Dr. Slamon's testimony appears consistent with surveys conducted by Genentech, [redacted]

52. Moreover, there is strong evidence that an ADCC and an anti-signaling effect are not mutually exclusive:

- Dr. Stern, a Genentech scientist, provided the following testimony:

[redacted]

[10] Dr. Slamon was represented by Genentech in his deposition.

[redacted]

- Dr. Sliwkowski, another Genentech scientist, provided similar testimony:

[redacted]

53. [redacted]

[redacted]

3. Entire Market Value Rule

54. I have been asked to consider whether the patent-related features are the primary basis for customer demand for Herceptin in the Adjuvant Population. In particular, whether the demand for Herceptin in the Adjuvant Population is because it acts on ITCs and has an anti-

[11] The Court has also ruled that use of the antibodies claimed in the '752 Patent which result in both down regulation and ADCC or CDC is insufficient to preclude infringement. Ex. 38 [Order Construing Disputed Claim Terms of U.S. Patent No. 6,733,752, 5/9/2011 at 19–22].

signaling effect. Based upon my discussions with the University's technical experts, my review of deposition testimony of Genentech witnesses, and my review of Genentech external and internal marketing materials, I understand that there is strong evidence that these are necessary and important features of the efficacy of the drug in the Adjuvant Population, and therefore I conclude that the patent-related features of the '752 Patent are the primary basis for customer demand.

I also note that in the market for Herceptin, the specific mechanism of action is generally unimportant to consumers.

56. Dr. Robert Cohen, a Senior Fellow at Genentech,

. Dr. Mark Sliwkowski provided similar testimony.

. This testimony further supports the conclusion that in a hypothetical negotiation the Adjuvant Population would not be apportioned to into smaller subpopulations based on ADCC v. anti-signaling, or whether ITCs are detected as present, because this type of analysis does not drive the demand for the product.

57. If in a hypothetical negotiation Genentech had insisted on a royalty base limited to a subset of patients to approximate the number of patients in which ITCs are detected in a survey or excluding patients in which ADCC occurs exclusively (I have see no evidence that such a population exists, I am simply engaging a hypothetical), the University would have insisted on a royalty rate increase to offset any decrease in the size of the royalty base because the licensor would have recognized that sales to other patients were also predicated on efficacy in patients with

ITCs.[12] If patients were routinely tested for ITCs, and patients lacking detected ITCs were not treated, then, under these hypothetical circumstances, Genentech would have been justified in charging a higher price (thereby generating a higher profit) for product sold to such patients because the likely potential benefits would be extremely more valuable and, as a consequence, the royalty amount would also increase.

58. I understand that convoyed sales are sales of unpatented goods that are sold simultaneously with patented goods or otherwise as a result of the sales of patented goods, and may be considered in determination of the royalty base.[13] Genentech's witnesses and documentation consistently admit that Herceptin sales are driven by its activity on ITCs and that its anti-signaling effects that are a critical part of efficacy. For those patients in which anti-signaling or activity on ITCs may not be evidenced, the sales are still driven because of these attributes.

59. Although not necessary to my conclusions, I note that a number of the claims in the '752 Patent relate to the use of an anti-p185 antibody in combination with chemotherapy:

- Claim 9: The method of claim 1 further comprising administering to said individual an anti-tumor agent;
- Claim 14: The method of claim 10 further comprising administering to said individual an anti-tumor agent;
- Claim 15: The method of claim 9, wherein the anti-tumor agent is cis-platin; and,
- Claim 16: The method of claim 14, wherein the anti-tumor agent is cis-platin.

Dr. Stuart Aaronson has concluded that these claims are infringed when Herceptin is administered in the adjuvant setting according to the FDA-approved label.

60. The '752 Patent proposes that chemotherapy can be used in combination with the antibody to render the treatment more effective. The specification states that "[t]he prophylactic

[12] Because there is no established separate market for Herceptin adjuvant sales limited to patients with detected ITCs or excluding patients in which ADCC occurs exclusively, even if demand for Herceptin in the Adjuvant Population was not based upon its action on ITCs via an anti-signaling effect, in a hypothetical negotiation it would be still proper to use sales to the Adjuvant Population as the royalty base. An adjustment to reflect contribution of value, if any, would be made in the royalty rate.

[13] *Fujifilm Corp. v. Benun*, 605 F.3d 1366, 1373 (Fed. Cir. 2010).

compositions may include additional components to render them more effective," and then gives as an example using two antibodies, and using "anti-cancer agents, such as, for example, cis-platin." Ex. 1 ['752 Patent, col. 4:22-33].

Senior Oncology Fellow Dr. Robert Cohen indicated [redacted]

4. University-Genentech '311 Agreement

62. [redacted]

63. On January 9, 2004, [redacted]

[redacted] The '311 patent relates to "[a] method of treating certain mammalian tumors with monoclonal antibodies is provided. Monoclonal antibodies specific to distinct epitopes of p185, the translation production of the neu oncogene, are provided, and these are then contacted with the tumor antigen under conditions which allow binding of the antibodies to a degree sufficient to inhibit tumor growth. The monoclonal antibodies act synergistically thus enhancing their anti-tumorigenic effect upon the tumor. An injectable composition for treating certain mammalian tumors with monoclonal antibodies and methods for diagnosing mammalian cancer tumors which express the protein p185 on the surface of the cells are also disclosed." Ex. 61 ['311 patent].

[redacted] The '311 agreement [redacted]

[redacted] On November 24, 2010, the parties amended and clarified the terms of the agreement. Ex. 62 [Amendment No. 1 to 2004 License (amending Section 1.2(e))]. [redacted]

66. I understand that the '311 patent covers the commercialization of a treatment regimen comprising administration of trastuzumab and pertuzumab, another anti-HER2 monoclonal under development by Genentech. The 2004 License Agreement is informative to the hypothetical negotiation involving the '752 Patent.

67. The agreement involves a license to the '311 patent, all claims of which involve the combination of two antibodies. An example of the method claims is claim 1:

> 1. A method of treating mammalian cancer tumors having cells which express pl85 the translation product of the neu oncogene on their surfaces, comprising the steps of:

a) providing a first antibody specific for a first epitope on an extracellular domain of said translation product;

b) providing a second antibody specific for a second epitope on an extracellular domain of said translation product, the combination of said first and second antibodies being selected to produce synergistic inhibition of tumor growth; and

c) contacting said cells with said first and second antibodies under conditions which allow said first and second antibodies to bind to said translation product on the surfaces of said cells to a degree sufficient to inhibit the growth of the tumor.

An example of the composition claims is:

7. An injectable composition for treatment of a mammalian cancer tumor having cells which express pl85 the translation product of the neu oncogene on the surfaces of the cells, comprising

a) a first antibody specific to a first epitope on an extra- 5 cellular domain of said translation product;

b) a second antibody specific to a second epitope on an extracellular domain of said translation product the combination of said first and second antibodies being selected to produce synergistic inhibition of tumor 10 growth; and

c) a pharmaceutical acceptable injection vehicle.

68. Genentech agreed [redacted]

69. [redacted]

5. University-Novartis Agreement

70. [redacted]

71. [redacted]

[redacted]

The products covered by the University-Novartis agreement [redacted]

[redacted]

Afinitor(R) everolimus is approved for the treatment of patients with progressive neuroendocrine tumors of pancreatic origin, advanced renal cell carcinoma, and subependymal giant cell astrocytoma associated with tuberous sclerosis. Ex. 64 [Afinitor Prescribing Information]. [redacted]

75. The Novartis License Agreement is informative to the hypothetical negotiation involving the '752 Patent.

76. Norvatis agreed [redacted]

'447 patent.

77. [redacted]

V. SUMMARY OF OPINIONS REGARDING INDUCEMENT

78. I have also been asked by the University to review evidence in this case and provide an expert opinion on whether Genentech induced infringement of the '752 Patent claims.

A. Legal Standards

79. I have been asked to apply the following standards:

1. Literal Infringement

80. For literal infringement, I have been asked to assume that an accused process or product must contain each and every limitation of the asserted claim(s) or perform each step recited in the claim(s). I have been asked to assume that the claim language defines the scope of an invention, and that every limitation of a patent claim is material to whether something is covered by the claim. I also understand that infringement of dependent claims requires infringement of the independent claims from which they depend as well as infringement of any additional limitations present in the dependent claims. I understand that a "dependent" claim is a claim in the patent that incorporates another claim. An example of a dependent claim is claim 17 in the '752 Patent.

81. I have been asked to assume that that a product or process that does not literally infringe an asserted patent claim may nonetheless be found to infringe the claim under the "doctrine of equivalents" if there is "equivalence" between the elements of an accused product or process, on the one hand, and the elements of the patent claim, on the other.

2. Inducing Infringement

82. I have been asked to assume that a person who actively induces infringement of a patent is themselves liable as an infringer.

83. I have been asked to assume that to prevail on a claim for inducement, the University must establish that there has been direct infringement via the administration of Herceptin to the Adjuvant Population. I have also been asked to assume that the University must also establish that Genentech intentionally took actions that knowingly induce the direct patent

infringement. I have been asked to assume that the University must establish that Genentech had knowledge of the '752 Patent and a specific intent to cause the direct infringement through its acts.

84. I have been asked to assume that merely engaging in the acts that induce the infringement regardless of whether Genentech knows it is causing another to infringe is not sufficient.

B. Inducement

85. Genentech admits that it knew of the '752 Patent years before its infringement began. [redacted]

86. Genentech has asserted in this litigation that "Genentech formed the belief that it did not infringe claim 1 of the '752 Patent in or around 2005." Ex. 27 [4th Supp. Resp. Rog. 1]. Genentech cites to portions of Dr. Cohen's deposition in which he describes his own alleged analysis of the '752 Patent. *Id.* (citing Ex. 16 [Cohen Depo.] at 127-128).

87. I have been asked to render an opinion as to whether in my experience in the Industry a pharmaceutical company has ever relied on an "opinion" in the nature of that allegedly formed by Dr. Cohen to inform its views on whether it is practicing an issued United States patent. In my experience, I have never encountered any pharmaceutical company that has relied on an "opinion" such as that allegedly formed by Dr. Cohen.

88. Genentech's position that, as a company, it relied on the views of Dr. Cohen, in forming its position as to the '752 Patent is so inconsistent with the standard practice throughout the Industry that custom in the Industry would suggest that Genentech was hiding its true state of knowledge on the '752 Patent by pointing to Dr. Cohen's views.

89. Dr. Cohen is not a patent attorney. In addition, there are a large number of obvious deficiencies in his analysis. These deficiencies are described in detail in Dr. Aaronson's reports, and I incorporate his summary of those deficiencies in my declaration. *See* Ex. 66 [Aaronson Rpt.] Sect. XXV.A. For example, Dr. Cohen claims that Herceptin only acts on '752 Patent breast cancer cells but:

- Dr. Cohen spent essentially no time analyzing the '752 Patent;
- Dr. Cohen disclaimed expertise in the field and did not consult with experts;
- Dr. Cohen appears to have ignored evidence in his analysis;
- Dr. Cohen did not appear to have a clear understanding of malignant form and structure;
- Dr. Cohen did not perform a meaningful literature search; and,.
- Dr. Cohen claimed both to have considered images of ITCs but to not be able to interpret the images.

90. Dr. Cohen was not qualified to render a non-infringement opinion regarding the '752 Patent. Any individual in a position of any management authority at a pharmaceutical company in the Industry would immediately recognize and understand this fact. According to custom in the Industry, any analysis of the '752 Patent should have begun with analysis of the patent and its file history by a qualified patent professional supported by individuals with expertise in the field at issue. A formal procedure should have been instituted in which the analysis of the patent by the primary attorney was vetted by a more senior in house attorney, and then the consensus advice was provided to the responsible manager at the company. None of these basic criteria were satisfied by the Cohen "opinion."

91. I have been asked to provide an opinion regarding the following factors relating to Genentech's conduct as it relates to the '752 Patent:

- whether Genentech acted in a manner consistent with the standards of commerce for its industry;
- whether Genentech deliberately copied the ideas of the University;
- whether or not Genentech made a good-faith effort to avoid infringing the '752 Patent;
- whether the defendant relied on, or failed to proffer, any favorable advice or counsel; and,
- whether or not Genentech tried to cover up its infringement.

92. In my opinion Genentech has acted in a manner inconsistent with the customs in the Industry with regard to its infringement of the '752 Patent. For example, Genentech departed from the standard of commerce regarding obtaining licenses to patents necessary to ensure freedom to operate. As another example, it is a departure from custom in the Industry for Genentech to have relied on the unqualified opinion of Dr. Cohen.[14]

93. Dr. Aaronson's report describes extensive tracking of the research of Professor Drebin and Greene by Genentech. Aaronson Rpt. Sect. IX.B. I incorporate that discussion into my declaration. Based on my review of these facts, if a subordinate reported to me in my capacity as general counsel the facts regarding Genentech's tracking of the research of Professors Greene and Drebin, I would have concluded that copying occurred. Nothing in Genentech's reports or other evidence I have reviewed causes me to alter this conclusion.

94. I have seen no evidence that Genentech made a good faith effort to avoid infringing the '752 Patent. For example, I have seen no evidence of any efforts to design around the '752 Patent. *See also,* Ex. 16 [Cohen Depo.] at 354:23-355:9.

95. Genentech has not proffered favorable advice of counsel. To the contrary, there has been conduct that suggests a desire to hide evidence. For example, Dr. Cohen was listed in the original Rule 26 disclosure filed by Genentech on "[d]evelopment of Herceptin; prior art; state of the art," not on non-infringement. Ex. 67 [Genentech's Initial Disclosures]. In an interrogatory response seeking information on who at Genentech had read the '752 Patent, he was not even listed until November 1, 2011. Ex. 68 [Genentech's Supp. Resp. to Rog. 5]. Nonetheless, Genentech now claims to be relying on his views of the '752 Patent as its defense for infringement. Ex. 27 [Genentech's Supp. Resp. to Rog. 1].

96. As to whether Genentech has covered up its infringement, I note that Genentech distributed a version of what is known as the TNM System and that this is relevant to infringement. *See* Sharma Rpt, Sect. X. Genentech however did not produce a copy of the

[14] [redacted]

document until after the University had found out that the document had been generated and confronted Genentech with this fact. *See* Ex. 69 [10/18/2011 email string between counsel].

VI. GENENTECH'S JOINT DIRECT INFRINGEMENT

97. I have also been asked by the University to review evidence in this case and provide an expert opinion on whether Genentech has jointly infringed the asserted claims of the '752 Patent.

A. Joint Direct Infringement

98. I understand that direct infringement requires a party to perform or use each and every step or element of a claimed method. But a defendant cannot avoid liability for infringement by merely having another entity carry out claimed steps on its behalf. I have been asked to assume that a finding of joint infringement can be made upon a showing that the accused party has direction or control over the other party performing the claimed method steps, for example when there is an agency relationship between the parties who perform the method steps.

99. I conclude that there are instances in which Herceptin is administered in a way that Drs. Aaronson, Sharma, and Jensen have concluded infringes the '752 patent and that in these instances Genentech is a direct infringer. There are two aspects to the direct infringement: (a) Genentech's Access To Care Foundation administration of Herceptin to the Adjuvant Population; (b) Clinical studies that Dr. Sharma has concluded fall within the accused population and therefore are subject to the infringement analysis in the reports of Drs. Sharma, Aaronson and Jensen. See Sharma Decl., Paragraphs 24-25; Ex. 66 [Aaronson First Report]; Ex. 70[Sharma First Report]; Ex. 71 [Jensen First Report.]

B. Genentech Jointly Provides Treatment Through Its The Genentech Access To Care Foundation To Herceptin Patients In The Adjuvant Context

100. It is commonly understood in the Industry that a company can use third parties to act as their de facto agents to deliver health care services to patients, usually for the purposes of marketing or developing additional clinical data for use in marketing.

101. [redacted]

[redacted]

103. As Genentech executives have testified, GATCF is a program [redacted]

Doctors and patients contract with Genentech. [redacted]

[redacted]

[redacted] After a patient or doctor applies for aid, the GATCF screens the application to determine whether Genentech will sponsor treatment: [redacted]

According to Genentech's 2007 forecast model [redacted]

[redacted]

107. [redacted]

[redacted]

C. Genentech Jointly Conducts Studies Using The Infringing Method

108. [redacted]

[redacted]

[15] These are also referred to at Genentech as "company sponsored studies." Ex. 78 [Brammer Depo.] at 66:6-11, 66:18-67:11.

[redacted]

109. [redacted]

CSTs. Ex. 78 [Brammer Depo.] at 69:14-21.[16]

110. [redacted]

111. [redacted]

[16] It is my understanding that Genentech has failed to provide discovery detailing the CSTs ongoing or commenced after 2006 that involve the adjuvant use of Herceptin. For example, Genentech has failed to identify all of the CSTs involving the adjuvant use of Herceptin ongoing or commenced after 2006. Ex. 78 [Brammer Depo.] at 70:22-71:2. This is despite a Court order to provide a witness on "the purpose and nature" of such trials. Ex. 90 [9/19/11 Order].

[redacted] Ex. 78 [Brammer Depo.] at 213:19-214:7. The "investigator should conduct the study in accordance with the protocol and not make changes unless agreed to in advance in writing." *Id.* at 219:16-220:3; [redacted]

113. [redacted]

114. [redacted]

115. I have been asked to assume that under 35 U.S.C. § 271(e)(1) a safe harbor from patent infringement exists for activities solely for uses reasonably related to the development and submission of information under the Food Drug and Cosmetic Act.

116. [redacted]

117. As a preliminary matter, to my knowledge, Genentech has failed to provide the discovery necessary to support application of the safe harbor. Some of the studies with which Genentech is involved do not involve an Investigational New Drug exemption ("IND") or other FDA "filing[s]." Ex. 78 [Brammer Depo.] at 86:16-23; 97:17-24; 224:17-225:1; [redacted] Ex. 78 [Brammer Depo.] at 24:23-25:5; 86:24-87:13. She could not for example testify whether there were any Genentech-sponsored studies not submitted to the FDA: "Q. So are you aware of any studies that Genentech sponsors that are not recorded with the FDA?...THE WITNESS: I don't know…." Ex. 78 [Brammer Depo.] at 87:15-88:2. Genentech's corporate designee was also unable to identify the ISTs involving the adjuvant use of Herceptin which did not involve submission of the results to the FDA: "Q. …for investigator-sponsored trials, there may be studies that have been conducted relating to the adjuvant use of Herceptin where the results were not submitted to the FDA. You just don't know? A. I just don't know." Ex.78 [Brammer Depo.] at 100:1-6, 224:9-15

("…is it your understanding that there are ISTs that were commenced on or after November 2006 that were not intended to support approval for a new indication?...I do not know the specific status of each study in terms of the IND filing.").

118. [redacted]

119. [redacted] "There are investigator-supported studies for which a label submission is not made." Ex. 78 [Brammer Depo.] at 98:8-15. For ISTs, the principal investigator "makes the decision whether or not to file for an IND or whether it fits the FDA defined exempt status" and needs to notify Genentech as to what that determination is. *Id.* at 223:3-18; 228:17-24; Ex. 79 at -634. An example of such a notification letter is Ex. 85 (GNE00892230).

120. Genentech uses the results of its CSTs and ISTs for purposes other than *solely* for submission to the FDA. Genentech sometimes uses the results of studies to ensure the accuracy of its promotional materials. Ex. 78 [Brammer Depo.] at 113:23-114:6. Genentech also has marketing uses for its studies, including "maintain[ing] its leadership position in the adjuvant market." *Id.* at 161:7-162:4; Ex. 84 (GNE00461681-461722 at -710); Ex. 86 [GNE00543558-559]. One focus of the studies under Genentech's medical plan is to "maximize penetration and duration of treatment." Ex. 87 [GNE00814308-354 at -310]. Genentech's corporate designee on

supported studies confirmed that "penetration" is a marketing concern. Ex. 78 [Brammer Depo.] at 163:3-9.

121. In the Industry, post-approval studies are often used for commercial purposes even when the topic of the studies is outside of the approved indication.

122. [redacted] This study explores the efficacy of Herceptin in lower-HER2 overexpressers. Because Herceptin is already on the market, data from this study can be used to inform treatment decisions by doctors without any change to the FDA label. In other words, the study has a highly relevant commercial purpose completely separate from any regulatory obligations or interactions with the FDA.

[redacted]

124. [redacted] Because Herceptin is already available, this study can be used to inform treatment decisions by doctors without any change to the FDA label.[17] In other words, the study has a highly relevant

[redacted]

17 [redacted]

commercial purpose completely separate from any regulatory obligations or interactions with the FDA.

[redacted]

I declare under the penalty of perjury that the foregoing is true and correct. Executed in the Town of New Lisbon, Ostego County, New York State, on March 20, 2012.

Edward T. Lentz